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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/613,177	07/10/2000	Kuber T. Sampath	CIBT-P02-540	8978

28120 7590 11/19/2004

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EXAMINER	
FREDMAN, JEFFREY NORMAN	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 11/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/613,177	SAMPATH ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,13,15,30-33,36 and 43-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,13,15,30-33,36 and 43-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status

1. Claims 1-10, 13, 15, 30-33, 36, 43-50 are pending.

Claims 1-10, 13, 15, 30-33, 36, 43-50 are rejected.

Any rejection which is not reiterated in this action is hereby withdrawn as no longer applicable.

Double Patenting

2. Claims 1-10, 13, 15, 30-33 and 36, 43-50 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 5,834,188. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims are a species of the genus of the current claims, where the method of claim 2 of the U.S Patent is drawn to a species of screening using OP-1. The species anticipates the genus claim and renders the genus claim obvious.

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim Rejections - 35 USC § 102

4. The rejection of claims 1, 13, 36, 45-47, 49 and 50 under 35 U.S.C. 102(e) as being anticipated by Harris et al (U.S. Patent 6,083,690) is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 103

5. The rejection of claim 1, 13, 36, 43, 45-47, 49 and 50 under 35 U.S.C. 103(a) as being unpatentable over Harris et al (U.S. Patent 6,083,690) in view of Smart (U.S. Patent 5,650,276) is withdrawn in view of the amendment.

6. Claims 1-3, 6, 9, 13, 36, 43-47, 49 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al (U.S. Patent 6,083,690) in view of Smart et al (U.S. Patent 5,650,276) and further in view of Nadal-Ginard (WO 94/18239).

Harris teaches a method for identifying a compound that induces a BMP mediated biological effect (see column 51, claim 8 and column 4, lines 20-31, for example) comprising:

(a) providing a test cell comprising a DNA (see column 51, claims 5 and 6 and column 12, example 3) comprising:

(i) a transcription activating element responsive to said morphogen (see column 51, claim 1 and column 4, line 55 to column 5, line 35, where Harris expressly contemplates the use of promoters from genes including BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, as well as similar genes as shown by column 5, line 33)

(ii) a reporter gene encoding a detectable gene product, the transcription activation element being in operative connection with the reporter gene (see column 51,

claim 6 and claim 8 and column 4, line 63 to column 5, line 8, where the promoter from the morphogen responsive gene is operatively linked to reporter genes such as firefly luciferase, CAT or green fluorescent protein),

wherein the reporter gene is transcribed when the DNA is present in a cell that is

(1) responsive to the morphogen and (see column 51, claims 1-8 and column 5, lines 37-50, where Harris uses cells such as osteoblasts)

(2) contacted with said morphogen (see column 51, claim 8, where Harris expressly teaches screening for osteogenic agents).

(b) exposing the test cell to a candidate compound (see column 51, claim 8 and column 12, example 3).

(c) detecting expression of said detectable gene product (see column 51, claim 8 and column 12, example 3),

wherein an increase in expression of the detectable gene product after exposing the test cell to the candidate compound indicates that the ability of the compound to induce morphogen mediated biological effects wherein said morphogen-mediated biological effect requires the presence of said morphogen-responsive transcription activating element so as to thereby identify a compound that induces a biological effect mediated by a morphogen (see column 13, example 4, lines 15-25, where Harris shows that compounds which enhance expression have the ability to induce morphogen mediated biological effects.)

With regard to claim 13, Harris teaches synthesis of compounds (such as recombinant BMP-2) which induce morphogenic effects (see column 13, example 4).

With regard to claim 36, Harris teaches the screening method as described above and teaches detecting the DNA binding within "approximately" 2 hours (specifically somewhat more than 10 minutes as shown in column 12, lines 60-67, which meets the "approximately" 2 hour requirement given the broad scope of "approximately" 2 hours).

With regard to claim 45, Harris teaches the use of promoters from BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, as well as similar genes as shown by column 5, line 33.

With regard to claim 46, Harris teaches the use of human promoters (see column 6, lines 61-67).

With regard to claims 47 and 49, Harris teaches that the biological effect may include enhancing bone nodule formation (see column 13, example 4).

With regard to claim 50, Harris teaches that osteocalcin expression may be enhanced (see column 13, example 4).

While Harris expressly recognizes that the promoters from other, similar, genes can be used in the screening method, Harris does not specifically teach the use of the OP-1 gene.

Smart teaches an screening method wherein "The invention features a method of screening candidate compounds for the ability to modulate the effective local or

systemic concentration or level of morphogenic protein in an organism. (see column 2, lines 61-64)." Smart teaches the desirability of screening candidate compounds for their ability to modulate morphogenic proteins (abstract). Smart expressly teaches OP-1 and OP-2 derived from humans (see column 4, line 38). Smart teaches morphogenic effects such as stimulating proliferation of progenitor cells (See column 2, lines 26-59) including osteoblasts (see column 17, lines 35-36).

Harris in view of Smart teach the limitations of claims 1, 13, 36, 43, 45-47, 49 and 50 as discussed above. Smart expressly teaches that OP-1 is associated with cells in the muscle (see column 16, lines 31-33).

Harris in view of Smart do not teach the use of the MEF-2 or AP-1 elements, which are functional in muscle cells.

Nadal-Ginard teaches screening for agents which either enhance of decrease the interaction of MEF2 transcription factors as well as MyoD and MASH transcription factors (abstract).

Further, the sequences of Harris, Smart or Nadal-Ginard are all "variants" of the nucleotides disclosed in claim 30 and meet this limitation.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to apply the method of Harris, who specifically suggests the use of other promoters, to the screening of other compounds which induce morphogensis since Smart expressly notes the desirability of screening compounds for

their ability to modulate morphogenesis (see column 2, lines 61-64, abstract, column 15, lines 55-64, especially). So an ordinary practitioner, faced with the teaching of Harris that other promoters are of interest, would have been expressly motivated by Smart to study OP-1, which is shown by Smart as an important morphogenic protein. Smart teaches that it is desirable to screen compounds for the physiologic effect of morphogenesis. That is, an ordinary practitioner interested in determining which compounds would effect the physiologic pathway termed morphogenesis as motivated by Smart would have been motivated to apply the method of Harris to this analysis since Harris expressly suggests analysis of such pathways and since Harris clearly indicates that such screening can result in clinical and therapeutic advantages (see example 4).

Further, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to apply the method of Harris in view of Smart to the downstream screening of MEF2 related compounds for the study of differentiated tissue as taught by Nadal-Ginard since Nadal-Ginard states "The agents useful in the invention either enhance or decrease the interaction between a pocket protein, eg retinoblastoma protein and a tissue specific trasncription factor, eg members of the MyoD, MEF2 or MASH family of transcription factors" (abstract)." Nadal-Ginard further notes that "Applicant's discovery provides the basis for screening therapeutic agents useful for regulating the switch between the cell's growth phase and a terminally differentiated state (page 4, lines 18-20)". Thus, an ordinary practitioner would have been motivated by Nadal-Ginard to screen for compounds which are involved in

differentiation using the MEF2 transcription factor sites in view of Nadal-Ginard's express motivation to use these enzymes in screening between differentiation and growth.

7. Claims 1, 13, 36, 43, and 45-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al (U.S. Patent 6,083,690) in view of Smart et al (U.S. Patent 5,650,276) and further in view of Ozkaynak et al (U.S. Patent 5,652,118).

Harris in view of Smart teach the limitations of claims 1, 13, 36, 43, 45-47, 49 and 50 as discussed above.

Harris in view of Smart do not teach the association of N-CAM and morphogenesis.

Ozkaynak expressly teaches screening for candidate compounds which alter endogenous morphogen levels (see example 9, column 37-38) and Ozkaynak expressly teaches the association of N-CAM expression with morphogenesis (see column 29).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to apply the method of Harris in view of Smart to the screening of N-CAM related compounds since Ozkaynak states "The morphogens described herein induce CAM expression, particularly N-CAM expression, as part of their induction of morphogenesis (see column 29, lines 2-3)" and since Ozkaynak further states the desirability of compound screening in example 9.

Response to Arguments

8. Applicant's arguments filed November 5, 2004 have been fully considered but they are not persuasive.

Applicant does not traverse the double patenting rejection but also did not file a terminal disclaimer. Therefore, this rejection remains applicable.

Applicant argues that because the 103 over Harris in view of Smart falls, so does the further 103 in which Nadal-Ginard or Ozkaynak are applied. This is not correct since Nadal Ginard expressly teaches "The agent can affect, e.g., induce, or enhance, the expression of a pocket protein. (see page 17, lines 20-21)." So Nadal-Ginard expressly teaches the new requirement of an agent such as a morphogen, which induces the expression of a different protein. This is particularly exemplified in claim 4 of Nadal-Ginard, in which expression of a reporter construct is dependent upon interaction of a candidate agent with the promoter sequence of a downstream gene. Consequently, this 103 rejection is maintained.

Similarly, Ozkaynak teaches a downstream expression, here N-CAM, which is a promoter distinct from the gene encoding the morphogen.

Conclusion

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637
11/17/04